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August 21, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 99D-2636
Draft Guidance for Industry on
Levothyroxine Sodium

FDA recently published a list of guidance documents which are "currently in effect." 65 Fed. Reg. 45428 (July 21, 2000). The list includes two level one guidance documents, the first titled In Vivo Pharmacokinetics and Bioavailability Studies and In Vitro Dissolution Testing for Levothyroxine Sodium Tablets (the "Bioavailability Guidance"), the second titled Levothyroxine Sodium (the "Levothyroxine Guidance"), which were published as drafts in 1999. 64 Fed. Reg. 31280 (June 10, 1999) and 64 Fed. Reg. 44935 (August 18, 1999). My client, Knoll Pharmaceutical Company, submitted detailed comments on each of these draft guidances.[1]

According to FDA's notice on the Development, Issuance, and Use of Guidance Documents, 62 Fed. Reg. 8961 (Feb. 27, 1997), level one guidances are not supposed to progress from draft to final without the agency's reviewing all comments, nor are they supposed to progress from draft to final without the agency's announcing that the guidance is final and analyzing significant comments. Yet that seems to be exactly what has happened here. Two very important draft guidances seem somehow to have taken effect, even though the agency has not taken the steps it is supposed to have taken before draft guidances become final. Because these two levothyroxine documents are very important to manufacturers and marketers of these products, and because they contain significant errors of law, fact, and

1. Knoll's comments on the Bioavailability Draft Guidance were submitted in my August 2, 1999 letter to the docket and Dr. Robert W. Ashworth's August 6 letter to the docket. Knoll's comments on the Levothyroxine Draft Guidance were submitted in Dr. Ashworth's and Mr. Steven Goldberg's October 18, 1999 letter to the docket.

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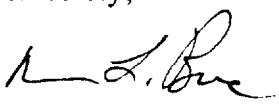
policy, it is important that neither the public nor the agency's staff be misled by the agency itself into relying on them as final when they are in fact still in draft.

Knoll therefore calls upon FDA either to make it clear that these two level one guidances are in fact still drafts, or, if they have somehow gone final, to withdraw them in accordance with the good guidance policy, which provides that if GGPs are not followed, the person with sign-off authority should withdraw the guidance document and reissue it in accordance with GGPs. Id. at 8968.

Sincerely,



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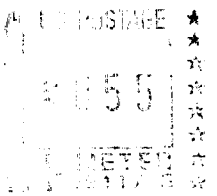

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